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PART VI

ENVIRONMENTAL PROTECTION AGENCY

Pesticide Programs

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REBUTTABLE PRESUMPTION AGAINST REGISTRATION AND CONTINUED REGISTRATION OF PESTICIDE PRODUCTS CONTAINING DIMETHOATE

ENVIRONMENTAL PROTECTION AGENCY

[OPP-30000 (FRL 787-6) 16]

PESTICIDE PROGRAMS

Rebuttable Presumption Against Registration and Continued Registration of Pesticide Products Containing Dimethoate

AGENCY: Office of Pesticide Programs, Environmental Protection Agency (EPA).

ACTION: Notice of rebuttable presumption.

SUMMARY: This notice provides public notification that dimethoate has been found to exceed certain risk criteria set forth in 40 CFR 162.11. The notice requests registrants and other interested persons to submit rebuttals and comments on the presumption and to submit any other data on the risks and benefits of dimethoate. This notice is the first of several which will give public notification of the Agency's progress in reviewing this chemical.

DATE: Comments must be received on or before November 7, 1977.

ADDRESS COMMENTS TO: Federal Register Section, Technical Services Division (WH-569), Office of Pesticide Programs, EPA, Rm. 401, East Tower, 401 M St. SW., Washington, D.C. 20460.

FOR FURTHER INFORMATION CONTACT:

W. T. Waugh, Office of Special Pesticide Reviews, Office of Pesticide Programs (WH-566), EPA (202-755-5851).

SUPPLEMENTARY INFORMATION: The Deputy Assistant Administrator, Office of Pesticide Programs, Environmental Protection Agency (EPA), has determined that a rebuttable presumption exists against registration and continued registration of all pesticide products containing dimethoate.[1]

I. Regulatory Provisions

A. *General.* Title 40, Part 162.11, of the Code of Federal Regulations for the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) as amended (86 Stat. 973, 89 Stat. 751, 7 U.S.C. 136 et seq.), provides that a rebuttable presumption against registration shall arise if the Agency determines that a pesticide meets or exceeds any of the risk criteria relating to acute and chronic toxic effects set forth in section 162.11 (a)(3). If it is determined that such a rebuttable presumption has arisen, the regulations require that the registrant be notified by certified mail and afforded an opportunity to submit evidence in rebuttal of the presumption. In addition, the Agency has determined that the public should also be given notice of the bases for the presumption to provide an opportunity for comment and to solicit additional information relevant to the presumption.

A notice of rebuttable presumption against registration is issued when the evidence related to risk meets the criteria set forth in section 162.11(a)(3). It is emphasized that a notice of rebuttable presumption against registration and continued registration of a pesticide is not a notice of intent to cancel the registration of a pesticide, and may or may not lead to cancellation. The notice of intent to cancel is issued only after the risks and benefits of a pesticide are carefully considered and it is determined that the pesticide may generally cause unreasonable adverse effects to the environment.

Accordingly, all registrants and applicants for registration are invited pursuant to 40 CFR 162.11(a)(4) to submit evidence in rebuttal of the presumptions listed in Part II of this notice and, in the case of oncogenicity, to submit information which relates to the assessment of oncogenic risks as set forth in the Agency's Interim Procedures and Guidelines for Health Risk and Economic Impact Assessment of Suspected Carcinogens (May 25, 1976; 41 FR 21402). Registrants and othere interested parties may submit for consideration data on benefits which they believe would justify registration or continued registration. In addition, any registrant may petition the Agency to voluntarily cancel a current registration pursuant to Section 6(a)(1) of FIFRA.

This notice of rebuttable presumption against dimethoate also describes scientific studies which suggest that dimethoate may cause delayed neurotoxicity and synergism of dimethoate by other pesticides, especially by EPN. The Agency is soliciting information and comment on these questions, but is not now presuming against on the basis of these studies.

B. *Rebuttal Criteria.* Section 162.11(a)(4) provides that a registrant may rebut the presumption by sustaining the burden of proving:

(1) In the case of a pesticide presumed against pursuant to the acute toxicity or lack of emergency treatment criteria, "that when considered with the formulation, packaging, method of use, and proposed restrictions on the directions for use and widespread and commonly recognized practices of use, the anticipated exposure to an applicator or user and to local, regional, or national populations of nontarget organisms is not likely to result in any significant acute adverse effects" [40 CFR 162.11(a)(ii)]; or

(2) In the case of a pesticide presumed against pursuant to the Chronic toxicity criteria, "that when considered with proposed restrictions on use and widespread and commonly recognized practices of use, the pesticide will not concentrate, persist or accrue to levels in man or the environment likely to result in any significant chronic adverse effects" [40 CFR 162.11(a)(ii)]; or

(3) In either case, that "the determination by the Agency that the pesticide meets or exceeds any of the criteria for risk was in error."

C. *Benefits Information.* In addition to submitting evidence to rebut the presumption of risk, Section 162.11(a)(5)(iii) provides that a registrant "may submit evidence as to whether the economic, social, and environmental benefits of the use of the pesticide subject to the presumption outweigh the risk of use." If the risk presumptions are not rebutted, the benefit evidence submitted by the registrant,[2] applicants, and other interested persons will be considered by the Administrator in determining the appropriate regulatory action. Specifically Section 162.11(a)(5)(iii) provides that if the "benefits appear to outweigh the risks," the Administrator may (1) issue a notice of intent to hold a hearing pursuant to Section 6(b)(2) of FIFRA rather than a notice of intent to cancel or (2) deny registration pursuant to Section 6(b)(1) of FIFRA. Alternatively, if the "benefits do not appear to outweigh the risks, the Administrator shall issue a notice pursuant to Section 3(c)(6) or Section 6(b)(1) of the Act, as appropriate." Moreover, if at any time the Administrator determines that a pesticide poses an "imminent hazard" to humans or the environment, a notice of suspension may be issued pursuant to Section 6(c) of the Act.

Stated below are the Section 162.11 (a)(3) risk criteria which the Agency has found to have been met or exceeded by registrations and applications for registration of pesticide products containing dimethoate. The Agency's basis for concluding that these risk criteria have been met or exceeded is set out in "Dimethoate: Position Document 1," which follows. Copies of attachments to the Position Document which are not published with this notice are available for

[1] A position document, containing an appendix of references, background information, and other material pertinent to the issuance of this notice, has been prepared by the Agency Working Group on dimethoate and is also published with this notice. This position document and its attachments are available for public inspection in the Office of Special Pesticide Reviews (WH-566), Office of Pesticide Programs, Environmental Protection Agency, East Tower, Room 447, 401 M Street SW., Washington, D.C. 20460.

[2] Registrants or other interested persons who desire to submit benefit information should consider submitting information on the following subjects, along with any other relevant information they desire to submit:

1 Identification of the major uses of the pesticide, including estimated quantities used by crop or other application.

2 Identification of the minor uses of the pesticide, including estimated quantities used by category such as lawn and garden uses and household uses.

3 Identification of registered alternative products for the uses set forth in (1) and (2) above, including an estimate of their availability.

4 Determination of the change in costs to the user of providing equivalent pesticide treatment with any available substitute products.

5 Assessment of regulation impact upon user productivity (e.g., yield per acre and/or total output) from using available substitute pesticides or from using no other pesticides.

6 If the impacts upon either user costs or productivity are significant, a qualitative assessment of the regulation's impact on production of major agricultural commodities and retail food prices of such commodities.

public inspection (see Footnote 1). Information protected from disclosure pursuant to FIFRA Section 10 cannot be provided. Specific inquiries concerning the Position Document should be directed to Project Manager W. T. Waugh, Office of Special Pesticide Reviews (WH-566), EPA, Rm. 447, East Tower, 401 M St. SW., Washington, D.C. 20460 (202-755-5851).

II. Presumptions

A. *Oncogenicity.* 40 CFR 162.11(a)(3)(ii)(A) provides that a rebuttable presumption shall arise if a pesticide "[i]nduces oncogenic effects in experimental mammalian species or in man as a result of oral, inhallation or dermal exposure * * *." As a further clarification of the provision, the preamble to the Agency's Interim Procedures and Guidelines for Health Risk and Economic Impact Assessment of Suspected Carcinogens (May 25, 1976; 41 FR 21402) states that "a substance will be considered a presumptive cancer risk when it causes a statistically significant excess incidence of benign or malignant tumors in humans or animals."

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that this risk index has been exceeded by all registrations and applications for registration of pesticide products containing dimethoate, and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

F. *Mutagenicity.* 40 CFR 162.11(a)(3)(ii)(A) also provides that a rebuttable presumption shall arise if a pesticide "* * * induces mutagenic effects, as determined by multi-test evidence." The Mutagenicity Testing Requirements Section of the FIFRA, Draft Section 3 Guidelines on Hazard Evaluation of Humans and Domestic Animals defines multi-test evidence as "evidence from at least two submammalian test systems in combination with evidence that the agent or its active metabolite(s) reaches the germinal tissue in mammals when administered by an appropriate route."

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that this risk index has been exceeded by all registrations and applications for registration of pesticide products containing dimethoate, and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

G. *Other Chronic or Delayed Toxic Effects.* 40 CFR 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise if a pesticide "[p]rodoces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety * * *."

On the basis of scientific studies and information summarized in the Position Document, the Agency has concluded that dimethoate can cause reproductive and fetotoxic effects in mammalian species and that this risk index has been exceeded by all registrations and applications for registration of pesticide products containing dimethoate, and that a rebuttable presumption against new or continued registration of such products has therefore arisen.

III. Grounds for Pesticide Review in Addition to Rebuttable Presumption Criteria

A. *General.* In addition to the risk criteria set forth in 40 CFR 162.11(a)(3) which require the issuance of a notice of rebuttable presumption against registration or continued registration and a determination by the Administrator to register or cancel a pesticide, 40 CFR 162.11(a)(6) provides that the Administrator may determine that a pesticide should be cancelled or that a hearing should be held if the pesticide poses a substantial question of safety to man or the environment "based on toxicological data, epidemiological studies, use history, accident data, monitoring data, or such other evidence as is available to the Administrator."

A determination to cancel or deny registration of a pesticide or to hold a hearing based upon such data and a finding that a pesticide poses a substantial question of safety need not be preceded by public notice and opportunity for rebuttal prior to the administrative adjudicatory hearing procedure of Section 6(b) of the Act. However, where the Agency is using a notice of rebuttable presumption against registration or continued registration based on the risk criteria of 40 CFR 162.11(a)(3), it is in the public interest to include all evidence which may indicate additional grounds for determining that a pesticide causes unreasonable adverse effects on the environment. Accordingly, evidence derived from studies which suggest that dimethoate may produce delayed neurotoxic effects and synergism of dimethoate by other pesticides, especially EPN, has been included in this notice.

B. *Delayed Neurotoxicity.* The information concerning the delayed neurotoxic effects of dimethoate is summarized in the Position Document. Demyelination studies for dimethoate on white leghorn hens appeared to show no myelin degeneration. However, deficiencies in the study's protocol, listed in the Position Document, caused concern that the study results were not conclusive. The Agency is not presuming against dimethoate on this basis but requests any interested party possessing information relevant to the delayed neurotoxicity of dimethoate to submit such data to the Agency.

C. *Synergism.* The information concerning synergism of dimethoate is summarized in the Position Document. (Synergism is defined as the greater toxicity of two compounds together than would be anticipated from the sum of their individual effects.)

Studies have shown that EPN can cause synergistic toxicity of dimethoate in mammals. The Agency is not now presuming against dimethoate on this basis but requests registrants and any other interested party possessing information relevant to the use of EPN with dimethoate, or to the synergism of dimethoate by EPN or any other pesticide to submit such data to the Agency.

IV. Registrations and Products Subject to the Notice

All registrants and applicants for registration listed below are being notified by certified mail of the rebuttable presumption existing against registration and continued registration of their products.

The registrants and applicants for registration shall have 45 days from the date this notice is sent or until November 7, 1977, to submit evidence in rebuttal of the presumption. However, the Administrator may, for good cause shown, grant an additional 60 days during which such evidence may be submitted. Notice of such an extension, if granted, will appear in the Federal Register.

V. Duty to Submit Information on Adverse Effects

Registrants are required by law to submit to EPA any additional information regarding any adverse effects on man or the environment which comes to a registrant's attention at any time, pursuant to Section 6(a)(2) of FIFRA and 40 CFR 162.8(d). If any registrant of dimethoate products has any published or unpublished information, studies, reports, analyses, or reanalyses regarding any adverse effects in animal species or humans, residues, and claimed or verified accidents to humans, domestic animals, or wildlife, which have not been previously submitted to EPA, the material must be submitted immediately. When responding to this notice, each registrant shall submit a written certification to the Agency that all information regarding any adverse effects known to the registrant has been submitted. In addition, the registrants should notify EPA of any studies currently in progress, including the purpose of the study, the protocol, the approximate completion date, and a summary of all results observed to date.

VI. Public Comments

During the time allowed for submission of rebuttal evidence, comments on the presumptions set forth in this notice and on the material contained in the Position Document are solicited from the public. In particular, any documented episodes of adverse effects to humans, domestic animals, or wildlife, and information as to any laboratory studies in progress or completed, are requested to be submitted to EPA as soon as possible. Specifically, information on the fate and effects of dimethoate, its impurities, metabolities, and degradation products on flora and fauna, particularly animals with metabolism similar to man, is solicited. Similarly, any studies or comments on the benefits from the use of dimethoate are requested to be submitted. All comments information received, as well as any other relevant information and

analysis thereof, which come to the attention of the Agency may serve as a basis for final determination pursuant to Section 162.11(a)(5).

All comments and information should be sent to:

Federal Register Section, Technical Services Division (WH-569), Rm 401, East Tower, 401 M Street SW., Washington, D.C. 20460

Three copies of the comments or information should be submitted if possible to facilitate the work of the Agency and others interested in inspecting them. The comments and information should bear the identifying notation "OPP-30000/16." Comments and information received within the specified time limit shall be considered before it is determnied whether a notice shall be issued in accordance with 40 CFR 162.11(a)(5)(ii).

Comments received after the specified time period will be considered only to the extent feasible, consistent with the time limits imposed by 40 CFR 162.11(a)(5)(ii). All written comments and information filed pursuant to this notice will be available for public inspection in the office of the Federal Register Section from 8:30 a.m. to 4 p.m. during normal working days.

Interested persons are encouraged to take advantage of the opportunity to inspect Agency files during normal working hours since (1) all of the information received may serve as a basis for final determination pursuant to Section 161.11(a)(5), and (2) the Agency will not generally publish a summary of information received in the FEDERAL REGISTER at the close of the rebuttal period.

Your cooperation is solicited in identifying any errors or omissions which may have been made in the following computer listings. Corrections to the listings may not necessarily be published in the FEDERAL REGISTER, but rather handled by mail with affected parties. Omissions will be corrected by notice in the FEDERAL REGISTER.

Dated: September 2, 1977.

EDWIN L. JOHNSON,
Deputy Assistant Administrator for Pesticide Programs.

DIMETHOATE: POSITION DOCMENT 1

(DIMETHOATE WORKING GROUP, U.S. ENVIRONMENTAL PROTECTION AGENCY)

DIMETHOATE POSITION DOCUMENT 1

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References.

DIMETHOATE: POSITION DOCUMENT 1

I. BACKGROUND

A. *Chemical, Physical Characteristics.* Dimethoate is an organophosphate insecticide. Its chemical name is O,O-Dimethyl S-(N-methyl-carbamoylmethyl) phosphorodithioate. Its structural formula is:

$$(CH_3O)_2P(S)SCH_2CONHCH_3$$

Dimethoate is a white, crystalline solid with a camphorlike odor. The technical grade material is a yellow-brown liquid. Dimethoate has a melting point of 51 to 52° C. It is most soluble in alcohols and ketones, as well as in organic solvents except saturated hydrocarbons. Its solubility in water is 2 to 3 percent (1, 2, 3). Dimethoate hydrolizes rapidly in alkaline solutions to a variety of products.[3] Dimethoate may be oxidized to a number of toxic products (cholinesterase inhibitors) by air, oxidative N-demethylation, and potassium permanganate.[4] An important metabolite is the toxic agent dimethoxon (the oxygen analog of dimethoate), formed when the sulfur in dimethoate is replaced by oxygen (1).

Dimethoate is a sulphur-containing organophosphorus insecticide which acts as an acetylcholinesterase inhibitor. The toxicity of dimethoate to animals depends, to a significant extent, on the conversion to the oxygen analog dimethoxon, [O,O-dimethyl-S-(N-methyl-carbamoylmethyl) phosphorothiolate] (5).

Hassan et al. (6) indicated that dimethoxon is 75 to 100 times more potent than dimethoate in inhibiting rat brain acetylcholinesterase. Lucier and Menzer (5) found dimethoxon to be 10^2 times more potent than dimethoate in inhibiting housefly head cholinesterase or human plasma cholinesterase, although dimethoxon was only four times more acutely toxic than dimethoate to houseflies in vivo.

The toxicity of dimethoate is related to purity. Very pure dimethoate contains little or no dimethoxon and is not as acutely toxic as technical dimethoate which contains more dimethoxon. Sanderson and Edson (7) found the acute oral LD_{50} of pure dimethoate to be 500 to 600 mg/kg for the male rat. The LD_{50} for technical dimethoate was 180 to 325 mg/kg for the male rat.

Since carcinogenic N-nitroso compounds may be produced by the reaction of nitrite with certain nitrogen compounds, the formation of N-nitroso derivatives as contaminants in pesticide formulations should be investigated whenever a potential nitrosatable substrate is involved. A literature search for work performed or work in progress yielded no data on potential N-nitroso dimethoate, and an Agency chemist concluded that "dimethoate would not be expected to give high yields of N-nitroso dimethoate" (51).

B. *Formulation and class.* Dimethoate is classed and used as a systemic insecticide/acaricide and is available in emulsifiable concentrates, soluble concentrates, ultra-low volume concentrates, wettable powders, and granules (1, 2). Formulations include a 5 percent granular, a 20 percent wettable powder, and 20 and 40 percent emulsifiable concentrates. It is especially effective against rasping and sucking pests.

C. *Registered uses and production.* Dimethoate has been produced as a pesticide since 1963. Thirty-eight registrants hold Federal registrations and manufacture 66 registered products. Sixteen companies have state registrations and produce[5] 34 products.

Environmental Protection Agency (EPA) records indicate that a total of 2,007,553 pounds of dimethoate was used in the United States during 1974 (8). Of this total, 9,455 pounds were used in industry; 5,443 pounds in government; and 1,992,655 pounds were used in agriculture. Of the agriculture total, 405,399 pounds were used on fruits and nuts; 383,233 pounds on sorghum; 294,955 pounds on corn; 254,896 pounds on vegetables; 193,205 pounds on cotton; 177,863 pounds on miscellaneous field crops; 175,751 pounds on livestock; 59,237 pounds on hay and small grains; 47,859 pounds on ornamentals, and 257 pounds on tobacco. (Additional uses are listed in Reference 9.)

The National Soils Monitoring Program (10), conducted by EPA's Ecological Monitoring Branch, has collected data on the application of dimethoate to various representative cropland sampling sites. The data indicated a limited use (<1 percent) of dimethoate. In fiscal year (FY) 1969, 0.12 percent (or two sites of out 1,684) reported using dimethoate. Average total application was 3.21 pounds/acre. There was no reported use of dimethoate on the cropland sampling sites in FY 1972. In FY 1973, 0.4 percent (or 6 sites out of 1,402) reported using dimethoate. Average total application was 0.58 pounds/acre. In FY 1974, 0.4 percent (or 5 sites out of 1,165) reported using dimethoate. Average total application was 1.63 pounds/acre. Among the crops to which dimethoate was applied were wheat, peppers, cotton, tomatoes, field corn, sorghum, grapes, oranges, and string beans.

D. *Tolerances.* Tolerances for total residues of dimethoate in or on raw agricultural commodities are listed in 40 CFR 180.204 as follows: 2 parts per million (ppm) in or on

[3] These products include desmethyldimethoate, O,O,dimethyl dithiophosphoric acid, O,O-dimethyl thiophosphoric acid, and dimethoate acid (the carboxy derivative (1).

[4] These toxic products include O,O-dimethyl S-(N-methylcarbamoylmethyl) thiophosphate, the N-demethylated analogs of dimethoate and dimethoxon and the N-hydroxmethyl intermediates of each, and dimethoxon (1).

[5] Pesticide products currently registered under state pesticide registration laws and shipped or distributed for sale solely within intrastate commerce are subject to Federal pesticide regulations under 40 CFR section 162.17(a).

alfalfa, apples, beans (dry, lima, snap), broccoli, cabbage, cauliflower, celery, collards, endive (escarole), grapefruit, kale, lemons, lettuce, mustard greens, oranges, pears, peas, peppers, soybean forage, soybean hay, spinach, Swiss chard, tangerines, tomatoes, turnips (roots and tops), and wheat (green fodder and straw); 1 ppm in or on corn fodder and forage, grapes, and melons; 0.2 ppm in or on potatoes and sorghum forage; 0.1 ppm in or on cottonseed, pecans, safflower seed, and sorghum grain; 0.1 ppm (negligible residue) in or on corn grain; 0.05 ppm (negligible residue) in or on soybeans; 0.04 ppm (negligible residue) in or on wheat grain; 0.02 ppm (negligible residue) in eggs and in meat, fat, and meat byproducts of cattle, goats, hogs, horses, poultry, and sheep; and 0.002 ppm (negligible residue) in milk. Dimethoate is registered for agricultural and home use.

E. *Metabolism.* Lucier and Menzer (5) investigated the nature of the oxidative metabolites of dimethoate formed in rats and on bean plants using radio-labeled dimethoate. In rats hydrolysis products predominated over chloroform-extractable metabolites. The oxygen analog, dimethoxon, was the major organo-extractable metabolite, and most of it had been extracted 6 to 12 hours after administration. Dimethoxon represented 5.39 percent of the administered radioactivity from males and 5.46 percent from females. Dimethoate was rapidly degraded in rats with only small quantities being recovered six hours after treatment. In bean plants the half-life of dimethoate was 1.7 days. At harvest, dimethoxon was the major organo-extractable metabolite, reaching a level of 7.33 percent after 3 days.

(1) *Absorption.* Shah and Guthrie (11) studied the absorption of ^{14}C-labeled dimethoate after 80 minutes through separately prepared sections of the digestive tract (small intestine, colon, rectum) of 6-week-old mice. On average, 50.9 percent of the applied dose had been absorbed in the serosal fluid and 14.2 percent in the gut tissue of the small intestine; 66.9 and 10.8 percent had been absorbed in the serosal fluid and gut tissue, respectively, of the colon; and 65.4 and 12.4 percent had been absorbed in the serosal fluid and gut tissue, respectively, of the rectum. When mice of different ages were tested, dimethoate penetrated more rapidly through the tissues of unweaned mice. The average absorbed in isolated sections of the small intestine after 80 minutes was 61.1 and 11.9 percent in the serosal fluid and gut tissue, respectively, for 12-day-old mice; 50.9 and 14.2 percent in the serosal fluid and gut tissue, respectively, for 6-week-old mice; and 56.5 and 13.7 percent in the serosal fluid and gut tissue, respectively, for 12-week-old mice.

(2) *Distribution.* Kaplanis et al. (12) analyzed tissues from an orally treated calf and showed only very low levels (0.02 ppm) of organo-extractable radioactive compounds present in brain, liver, testes, and lungs.

Chamberlain et al. (13) studied the metabolism and associated residues following intramuscular (i.m.) injection and oral administration of P^{32}-dimethoate in sheep. Degradation was rapid and appeared not to be significantly affected by the route of administration. Only trace residues were found in tissues of sheep sacrificed 2 and 4 weeks after treatment. The thio-carboxy derivative was the predominant degradation product found in samples of urine and accounted for one-fourth to one-half of the administered dose for all animals. When dimethoate was given orally at two dosage levels, it was noted that at the lower level the organosoluble fraction in the blood accounted for less than 5 percent of the total radioactivity, whereas at the higher level this fraction was above 30 percent. The authors suggested that the mechanism of breakdown was overwhelmed by the larger dose, allowing more dimethoate and dimethoxon to accumulate in the blood.

Dedek and Schwarz (14), using in vivo tests of dimethoate in cattle, reported <5 ppm dimethoate in the blood at 6 hours following a 20 mg/kg i.m. dose, >3 ppm at 12 hours, and about 2 ppm at 18 hours. Blood concentrations following a 15 mg/kg dermally applied dose of 2 percent dimethoate in a mineral oil solution were about 1 ppm at 6 hours, and almost zero at 12 hours. With a 20 mg/kg dermal dose of a 5 percent dimethoate/fatty oil solution, blood concentrations were about 2.5 ppm at 6 hours, 1.5 ppm at 12 hours, and about 1 ppm at 18 hours.

(3) *Biotransformation.* Lucier and Menzer (4) investigated the metabolism of dimethoate in bean plants. The metabolism of dimethoate-^{32}P and dimethoate-carbonyl-^{14}C was studied using four modes of application. Degradation occurred most rapidly in excised leaves, followed by stem-injected plants, root-treated plants, and least rapidly in plants treated by foliar application. Eighteen metabolites of dimethoate, including 11 unknowns, were isolated. The oxygen analog (dimethoxon) was consistently present in moderate amounts in plants treated by all four modes of applicaton. Oxidation of dimethoate took place to a lesser degree than hydrolysis, although oxidation seemed more important in foliar-treated plants than in the other modes of application.

Kaplanis et al. (12) studied the metabolism of dimethoate in cattle. Ten mg/kg P^{32}- of dimethoate was administered orally and by intramuscular injection. Eighty to 90 percent of the oral dose was eliminated in the urine after 24 hours, and the same percentage of the intramuscular dose was excreted after 9 hours. The major metabolic products were dimethyl phosphate, dimethyl phosphorothioate, and several unknowns.

Krueger et al. (15) studied the persistence and metabolism of dimethoate, among other compounds, to determine their toxicity to the mouse, American cockroach, and housefly. The observed selectivity of dimethoate for insects as compared with mammals was attributed to a persistence of unaltered parent compound in the whole body. In the mouse, 89 percent of a 0.5 $\mu g/g$ dose and 76 percent of a 30 $\mu g/g$ dose appeared in chloroform inextractables within 0.5 hours after treatment. The oxygen analog levels were approximately three times greater in the cockroach than in the mouse. The authors concluded that the mouse degrades either the parent compound or the oxygen analog more readily than the insect does, and that selectivity is probably due to differences in ability to degrade.

Uchida and O'Brien (16) studied the degradation of dimethoate by homogenates of human liver. An average of 0.27 $\mu g/g$ was degraded in a 30-minute period. Using this and other data available on dimethoate's acute toxicity, the authors suggested a probable acute oral LD_{50} to humans of approximately 30 mg/kg.

(4) *Excretion and degradation.* Kaplanis et al. (12) studied the metabolism of P^{32}-dimethoate in cattle following oral and i.m. administration of 10 mg/kg. About 87 to 90 percent of the oral dose was eliminated in the urine after 24 hours. The same percentage of the i.m. dose was excreted after 9 hours. Only 3.7 to 5 percent of the oral dose and about 1.1 percent of the i.m. dose were eliminated in the feces. The major metabolic products were dimethyl phosphate, dimethyl phosphorothioate, and several unknowns.

Brady and Arthur (17) studied the excretion of P^{32}-dimethoate in rats. Rats excreted about 45 percent of the orally administered dimethoate in the urine and only about 5.8 percent in the feces 72 hours after treatment. Rats treated dermally with dimethoate excreted 30.6 percent in the urine and 6.5 percent in the feces.

Rowlands (18) studied the metabolism of dimethoate by stored wheat and sorghum grains. Samples of both grains were treated with 2 or 10 ppm of dimethoate. Samples were analyzed after 1, 4, 7, 11, 14, and 21 days of storage. Dimethoate was rapidly degraded to anionic derivatives which the author considered nontoxic. Slight oxidation to dimethoxon occurred, but this was similarly degraded.

F. *Residues.*—(1) *Food.*—(a) *FDA commodity survey.* The Food and Drug Administration (FDA[6] has been collecting food and feed samples for a number of years, analyzing each sample to determine pesticide residue levels and frequency of occurrence (19). The following list indicates the commodities, the number of positives within the year, and the fiscal years (FY) when found contaminated. Figures include residues of both dimethoate and its oxygen analog for both domestic and imported products.

Commodity	Fiscal year		
	1974	1975	1976
Leaf and stem vegetables	4	3	32
Beans	19	8	26
Vine and ear vegetables	72	69	158
Large fruits	0	2	11
Small fruits	0	48	2
Root vegetables	0	1	0
Processed fruit products	0	11	2
Processed vegetable products	0	1	0
Total number occurrences	95	143	251

(b) *Other studies.* Dedek and Schwarz (14) reported residues in milk of dimethoate-treated cows. With a 20 mg/kg i.m. dose, dimethoate residues in milk were >3.5 ppm at 12 hours, <1 ppm at 24 hours, and <0.5 ppm at 36 hours. With a 15 mg/kg dermal dose of a 2 percent dimethoate/mineral oil solution, residues in milk were about 2.5 ppm after 1 to 2 hours, <1 ppm at 6 hours, and almost zero shortly after 12 hours. With a 20 mg/kg demal dose of a 5 percent dimethoate/fatty oil solution, residues in milk were almost 2 ppm at about 10 hours, about 1.5 ppm at 12 hours, and <0.5 ppm at 24 hours. The approved tolerance for dimethoate residues in milk is 0.002 ppm.

Steller and Brand (20), using gas-liquid chromatography, analyzed field-treated grape samples harvested 28 days after the last application of dimethoate. The authors reported residue values of <0.05 ppm of what appeared to be de-N-methyl dimethoate (O,O-Dimethyl S-carbamoylmethyl phosphorodithioate), N-hydroxymethyl dimethoate, de-N-methyl dimethoxon, and N-hydroxymethyl dimethoxon. The authors concluded that residue values demonstrated

[6] The U.S. Department of Agriculture conducts a comparable residue study for domestic and imported meat products. In 1973 and 1974, standard screening tests for organophosphate pesticides were conducted, but no dimethoate residues were found. Screening for organophosphate pesticides was discontinued in 1974.

degradation of dimethoate residues from a maximum of 18 ppm to approximately 0 5 ppm with no accumulation of dimethoxon (maximum of 0 3 to 0 4 ppm) The approved tolerance for dimethoate residues on grapes is 1 ppm.

(2) *Feed.* Beck et al (21) studied the persistence of dimethoate residues on soybeans, corn, and coastal bermudagrass. Dimethoate was sprayed at rates of 4, 8, and 16 ounces (of a formulation containing 43.8 percent dimethoate) per acre Residues degraded to the 0 1 ppm level about 7 and 16 days after treatment on soybeans and corn, respectively The same level was not reached in 70 days with bermudagrass (The authors suggested that lack of rainfall and the cool season of the year resulted in the extended persistence of residues on bermudagrass.) The approved tolerance levels for soybean and corn forage are 2 and 1 ppm, respectively

(3) *Plants.* Dauterman et al (22) analyzed surface and absorbed residues following foliar treatment of various crop plants with radioactive dimethoate in a solution equivalent to 0.5 pound of dimethoate per 100 gallons of water Dimethoate was rapidly absorbed. It decomposed both on the surface and inside the foliage. Only trace amounts of dimethoate and dimethoxon were present, 32 days after treatment in and on foliage of corn and peas. After 32 days, residues ranged from 16 to 39 ppm in and on foliage of four groups of potatoes, and 5 to 10 ppm in and on cotton.

(4) *Soil.* Bohn (23) studied the decomposition of dimethoate following the application (one pound actual per acre) of an emulsifiable concentrate to a cultivated sandy loam soil. Dimethoate disappeared rapidly, even when applied in amounts exceeding the recommended rate. Half of the insecticide in the top three inches of soil disappeared in four days under drought conditions and in 2.5 days after moderate rainfall. The rate of disappearance did not change with repeat applications.

Mishra and Gupta (24) studied the persistence of dimethoate in three types of soil sandy, loam, and clay loam. Dimethoate was applied at 4 and 8 ppm. After treatment, soil samples were drawn at 0, 1, 3, 5, and 7 days and thereafter every week for 5 weeks. Samples were taken from depths of 0 to 2 inches, 2 to 4 inches, and 4 to 6 inches. Dimethoate had a half-life of 5 to 7 days in sandy soil and loam at both 4 and 8 ppm at depths of 0 to 2 inches, as well as in sandy soil at 4 ppm at the 2–to–4–inch depth. Dimethoate had a half-life of 7 to 14 days at 4 ppm in loam and clay soil at depths of 2 to 4 inches, and 0 to 2 inches, respectively; and at 8 ppm in sandy, loam, and clay soil at depths of 2 to 4 inches, 2 to 4 inches, and 0 to 2 inches, respectively. A half-life of 14 to 22 days was recorded only for clay at the 2–to–4–inch depth at both 4 and 8 ppm. On day 5, the highest residues were recorded for all 3 soils at the 4–to–6–inch depth.

Duff and Menzer (25) studied the persistence and degradation of ^{14}C-dimethoate in silty loam, loamy sand, and clay loam. No major difference in total applied radioactivity recovered was noted between the three soil types in two experiments. Soil moisture content promoted more rapid disappearance of the dimethoate-^{14}C-equivalents.

Getzin and Rosefield (26) measured dimethoate residues by gas-liquid chromatography two weeks after application to Chehalis clay loam. Dimethoate degraded at about the same rate in heat-sterilized and gamma-irradiated soil, 18 and 20 percent, respectively. About 77 percent of the dimethoate had degraded after 2 weeks in nonsterile soil.

Harris and Hitchon (27), in laboratory tests on the biological activity of several pesticides in soil, reported dimethoate to be "moderately persistent," i e , its biological activity disappeared after 36 weeks.

There is apparently no substantial movement of dimethoate in soil Bohn (23) reported that rainfall did not cause appreciable leaching into the 3-to-6-inch zone of soil Mishra and Gupta (24) reported more leaching of dimethoate in sandy than in loam or clay-loam soils Duff and Menzer (25) reported that downward movement of dimethoate was slightly more extensive in loamy sand than silty loam or clay loam, and that increased moisture content in soil promoted downward movement in silty loam, loamy sand, and clay loam.

Duff and Menzer (25) also reported that in moist soils the conversion of dimethoate to dimethoxon was faster, and the levels of dimethoxon were generally greater The only hydrolytic metabolite of dimethoate they identified was dimethoate carboxylic acid.

Harris and Hitchon (27) studied the biological activity of several insecticides in soil. As already noted, dimethoate became inactive after 36 weeks. In dry sandy loam, 50 ppm was the lowest concentration at which dimethoate showed biological activity when applied as a soil treatment; in moist sandy loam the level was 10 ppm; and in muck the level was 100 ppm. The reported increase in toxicity (cholinesterase inhibition) of dimethoate in moist soil, as compared to dry sol, is probably due to the greater production of the toxic oxygen analog, dimethoxon, (see Duff and Menzer above). Dimethoate and its metabolites rapidly disappeared from highly saturated muck soil .

(5) *Air and water.* The National Air Monitoring Program (10), conducted by EPA's Ecological Monitoring Branch, does not have air data on dimethoate available since air samples are not being analyzed for this pesticide.

The National Estuarine Monitoring Program (10), also conducted by EPA's Ecological Monitoring Branch, does not have estuarine data on dimethoate.

(6) *Transport.* Graham-Bryce (28) studied the diffusion characteristics of dimethoate in silty loam soil. Diffusion rates varied little as the dimethoate concentration was increased; however, diffusion rates increased rapidly as the soil moisture increased. These findings agree with studies already cited in section I.F.(4) which showed little movement of dimethoate in soil, except under moist conditions (25, 27).

G. *Pesticide Episode Review System (PERS) Reports.* The Agency maintains a Pesticide Episode Review System, which collects reports of pesticide exposure affecting humans, domestic animals, livestock, and wildlife. For the period 1966 to June 1976, PERS data show a total of 50 episodes involving dimethoate (29) Thirty-five involved dimethoate alone, and 15 involved dimethoate in combination with other active ingredients.

Humans were affected in 38 of the 50 reported episodes, livestock in two, plants in one, fish in one, and environmental contamination in eight.

Site of occurrence was reported as agricultural operations in 28 of the 50 reported episodes, transportation in five, greenhouses in three, storage areas in two, homes in two, aerial application preparation sites in two, formulation plants in one, an unspecified urban worksite in one, and a disposal site in one. In addition, two episodes simultaneously involved both a residential area and a worksite. Three episode reports did not specify a site of occurrence.

For five of the 50 episodes, there was substantial evidence that dimethoate was directly involved; for 12 episodes, there was circumstantial evidence, for 31 episodes, there was insufficient evidence, and for two episodes, there was evidence which proved that dimethoate was not responsible for the episode.

For the 17 episodes in which there was either substantial or circumstantial evidence for dimethoate's involvement, 12 involved humans, two involved building contamination, and one each involved livestock, water contamination, and both water and soil contamination. Of the 12 human incidents, site of occurrence was reported as agricultural operations in four, homes in two, aerial application sites in two, and transportation, a greenhouse, a formulation plant, and a residential worksite area in one each The two building contaminations occurred in a greenhouse and a storage area. The livestock incident involved an agricultural operation, the water contamination involved a storage area; and the water and soil contamination involved a disposal site.

II. REGULATORY HISTORY

Dimethoate has been the subject of several Federal regulatory actions since its original registration. All actions were initiated when the U.S. Department of Agriculture was responsible for the regulatory control of pesticides.

Pesticide Registration (PR) Notice 67–10 issued on November 6, 1967, extended certain "no residue" and "zero tolerance" registrations beyond December 31, 1967. Uses of dimethoate were extended until January 1, 1969. (This and all following PR Notices are cited in Reference 30.)

PR Notice 68–3 isued on January 10, 1968, classified certain chemical use patterns as nonfood uses. For dimethoate, this included the use on agricultural premises, except in dairy barns and poultry houses.

PR Notice 68–5 issued on January 30, 1968, extended certain "no residue" and "zero tolerance" registrations beyond December 31, 1967. For dimethoate, uses in dairy barns and poultry houses were extended until January 1, 1969.

PR Notice 68–17 issued on November 1, 1968, extended certain "no residue" and "zero tolerance" registrations beyond December 31, 1968. For dimethoate, uses on alfalfa, cotton, and safflower, and in dairy barns and poultry houses were extended until January 1, 1970.

PR Notice 69–2 issued on January 16, 1969, extended certain "no residue" and "zero tolerance" registrations beyond December 31, 1968. For dimethoate, uses on potatoes and watermelons were extended until January 1, 1970.

PR Notice 70–1 issued on January 19, 1970, extended certain "no residue" and "zero tolerance" registrations beyond December 31, 1969. For dimethoate, use on alfalfa was extended until January 1, 1971.

III. SUMMARY OF SCIENTIFIC EVIDENCE TO SUPPORT REBUTTABLE PRESUMPTION

The following adverse effects of dimethoate have been found to exceed the criteria for issuance of a rebuttable presumption.

A. *Chronic Toxicity.*—(1) *Oncogenic Effects in Test Animals.* 40 CFR Section 162.11 (a)(3)(ii)(A) provides that "a rebuttable presumption shall arise if a pesticide's ingredient(s) * * * (i)nduce(s) oncogenic effects in experimental mammalian species or in man as a result of oral, inhalation, or dermal exposure * * *." Section 162.3 (bb) defines the term oncogenic as "the property of a substance or a mixture of substances to

produce or induce benign or malignant tumor formation in living animals."

The Office of Special Pesticide Reviews has conducted an exhaustive search of the open literature and has isolated two published research papers dealing with oncogenicity of dimethoate.

(a) *Studies Relevant to Rebuttable Presumption.* Gibel et al. (31) studied the effects of dimethoate on 10-week-old Wistar rats of both sexes. Forty animals per group were employed in the study. Fresh solutions of dimethoate were made at the time of administration to limit hydrolysis. The compound was given by gavage twice weekly at 5, 15, and 30 mg/kg dose levels. One group of animals was also given 15 mg/kg intramuscularly. The authors described technical dimethoate as a yellow-brown oil. Meister (2) described dimethoate as a white crystalline solid. The Working Group has requested a sample of the material used by Gibel et al.

Animals were weighed at regular intervals. Only the animals that lived 3 months in the study and showed no post mortem changes were examined histologically. Blood and bone marrow were also examined.

Treated animals showed strong hyperplasia of the blood forming parenchyma of the bone marrow involving erythropoesis, granulopoesis, and magakaryopoiesis. Nonbony myeloid metaplasia was seen primarily in the liver and spleen in 59 percent of the treated animals. In addition, granulocytosis was found in 22 percent of the animals.

Incidence of benign and malignant tumors shown in Table 1 indicates that there is a significant increase of malignant tumors among treated animals at the highest dose levels for both oral and intramuscular routes of administration.

TABLE 1.—*Incidence of tumors in rats treated with dimethoate*

Dose milligrams per kilogram	Route	Average survival (days)	Benign tumors	Malignant tumors	p values
0	Oral	473	3/36	0/36	
5	do	518	7/26	2/26	
15	do	511	5/25	3/25	
30	do	627	2/20	[1] 4/20	0.0132
0	1 im	711	4/35	0/35	
15	1 im	570	5/30	[2] 6/30	.0072

[1] 1 liver sarcoma, 1 malignant reticulosis, and 2 sarcomas of the spleen.
[2] 1 sarcoma of the spleen, 1 soft tissue sarcoma, 1 ovarian sarcoma, 1 reticulum cell sarcoma, 1 spleen sarcoma, and 1 liver sarcoma.

In addition, a significant linear trend ($p<0.01$) was found for the oral route. No significant difference was detected for benign tumors.

Gibel et al. (31) also studied the effects of dimethoate on mice. Percutaneous application of fresh solutions of dimethoate was given twice a week for six weeks on shaved back skin of AB mice of both sexes; the animals survived for only 270 days. Five animals out of 19 showed malignant tumors, of which there were four leukoses and one breast carcinoma. The spleen showed considerable metaplasia with often complete atrophy of white pulp. The follicles of the white pulp showed a loose, narrow lymphocytic mantle around the central arteries. The trabecular framework of the spleen was generally narrowed and reduced. The red pulp showed a partially localized, and diffuse myeloid proliferation with numerous immature cell forms which made it difficult to recognize the basic structure. The authors felt that mice also developed the myeloproliferative syndrome similar to that observed in rats.

The benign tumors observed in the control animals were exclusively fibroadenoma of the breast. The authors did not mention the incidence of malignant tumors in controls but implied that they did not find any malignant tumors in the control animals.

In 1977 the National Cancer Institute (NCI) completed a feeding study with dimethoate (32). Osborne-Mendel rats, 35 days old, were used as test animals. The compound was added to the diet at 250 and 125 ppm dose levels. After 19 days the doses were reduced to half and the treatment was continued for an additional 61 weeks. The animals were followed for 115 weeks. The treatment groups consisted of 50 animals of each sex, and the matched controls consisted of 10 animals. Matched controls for aldrin, chlordane, dichlorvos, dieldrin, and heptachlor were used for evaluation because these studies were carried out concurrently with the dimethoate feeding study. Complete histopathology was carried out on all the animals. Statistical analysis of tumor incidence by site and type indicated no excess incidence of any specific tumor type and also no increase in total tumor incidence. A summary of the survival data and number of tumor-bearing animals is shown in Table 2.

TABLE 2.—*Dimethoate chronic feeding study—number and survival of tumor-bearing rats*

Sex	Dosage group	Effective number [1]	Number TBA [2]	Percent	Percent surviving [3] (weeks)		
					52	78	[4] 115
Male	Pooled control	58	36	62	92	87	47
Do	Matched control	10	7	70	100	80	30
Do	Low	50	23	46	98	96	72
Do	High	49	24	49	92	82	58
Female	Pooled control	60	43	72	97	95	73
Do	Matched control	10	7	70	100	100	90
Do	Low	47	30	64	98	92	74
Do	High	45	21	47	88	67	51

[1] Total number of rats initially placed on test minus the number missing or autolyzed.
[2] Number of tumor-bearing rats.
[3] Denominator for survival percentages was the original number of animals minus those killed for diagnostic purposes. No animals were accidentally killed, and none were missing.
[4] Study terminated at 115 weeks.

The pathological evaluation of this study was done at Gulf South Research Institute. EPA's Carcinogen Assessment Group (CAG) is interested in reviewing the slides of this study.

NCI (32) also studied the effects of dimethoate on B6C3F hybrid mice which were 35 days old. The compound was added to the diet at 250 and 500 ppm dose levels, and the feeding was continued for 69 and 60 weeks, respectively. Animals were observed for additional 24 and 34 weeks, respectively, before sacrifice. All the animals were necropsied and examined histopathologically. The data were statistically analyzed for each organ and tumor type. No dose-related increase in tumor incidence by site or total in either sex was found. The data for total tumor-bearing animals are summarized in Table 3.

The pathological evaluation of this study was carried out at Gulf South Research Institute. CAG is interested in reviewing the slides of this study.

CAG (33) reviewed the results of both the Gibel et al. (31) and the NCI (32) studies and concluded, "The Gibel et al. study showed a statistically significant increase in malignant tumors and myeloproliferative syndromes in Wister rats tested orally or intramuscularly with dimethoate. * * * They also reported an increase incidence of malignant tumors and myeloproliferation in AB mice following percutaneous application of dimethoate on shaved back skin but the inadequate description of this part of the study precluded statistical analysis. The NCI study on dimethoate using different strains of rats and mice was negative. * * *"

TABLE 3.—*Dimethoate chronic feeding study—number and survival of tumor-bearing mice*

Sex	Dosage group	Effective number [1]	Number TBA [2]	Percent	Percent surviving [3] (weeks)		
					52	78	[4] 90
Male	Pooled control	96	31	32	94	92	85
Do	Matched control	7	6	86	100	100	86
Do	Low	50	11	22	98	84	82
Do	High	50	11	22	96	96	92
Female	Pooled control	80	14	18	96	90	83
Do	Matched control	10	3	30	90	90	70
Do	Low	50	15	30	96	96	90
Do	High	49	12	24	94	94	90

[1] Total number of mice initially placed on test minus the number missing or autolyzed.
[2] Number of tumor-bearing mice.
[3] Denominator for survival percentages was the original number of animals minus those killed for diagnostic purposes. No animals were accidentally killed, and none were missing.
[4] Study terminated at 90 weeks.

The Working Group concludes that the Gibel study on rats supports the issuance of a rebuttable presumption on the basis of oncognic effects for the following reasons. First, the studies on rats conducted by NCI and Gibel et al. were dissimilar in several ways. The test animal used by Gibel et al. was the Wistar rat, whereas NCI used the Osborne-Mendel rat. It is generally recognized (34) that different strains of test animals, for a variety of reasons, may demonstrate a varied response to a chemical. The method of application also varied in the two tests. NCI incorporated dimethoate in feed for the rat study whereas Gibel et al. administered dimethoate by intubation or intramuscular injection. Different methods of application may or may not result in a different response on the part of the test animal. Second, the purpose of the RPAR process is not to determine whether dimethoate is or is not an oncogen, but to determine whether there is sufficient information available to raise a question as to its safety in this regard. For these reasons the Working Group recommends that a rebuttable presumption be issued against dimethoate pursuant to 40 CFR Section 162.11 (a) (3) (ii) (A).

(b) *Studies On Which Further Information Is Sought.* Steiglitz et al. (35) studied the hematotoxic effects of dimethoate in rats. Dimethoate was administered to 10-week-old Wistar rats in doses of 5, 10, and 15 mg/kg body weight by oral intubation (p.o.). Another group was given an i.m. dose of 15 mg/kg. Each test group consisted of 40 animals with two control groups of 40 animals each. The most important hematological results included pronounced hyperplasia of the hematopoietic parenchyma in the bone marrow, and sometimes strong, extraosseous myeloid metaplasia. Hyperplasia in the bone marrow occurred at different levels in all three hematopoietic cell systems with preferential involvement of granulocytopoiesis. Leukocytosis of varying intensity in the peripheral blood was also found but mainly affected granulocytes. The highest value exceeded 50,000/ul.

The Agency is not now presuming against dimethoate on the basis of this study, but requests any interested party possessing information relevant to this or any other oncogenic effect due to dimethoate to submit such data to the Agency.

(2) *Mutagenic Effects.* 40 CFR Section 162.11(a)(3)(ii)(A) provides that "a rebuttable presumption shall arise if a pesticide's ingredient(s), metabolite(s), or degradation product(s) * * * induce mutagenic effects, as determined by multi-test evidence."

The Mutagenicity Testing Requirements Section of the FIFRA, Draft Section 3 Guidelines on Hazard Evaluation of Humans and Domestic Animals defines multi-test evidence as "evidence from at least two submammalian test systems in combination with evidence that the agent or its active metabolite(s) reaches the germinal tissue in mammals when administered by an appropriate route."

(a) *Studies on Dimethoate-Induced Mutations in Sub-Mammalian Test Systems.* Fahrig (36) treated cultures of *Saccharomyces cerevisiae*, with dimethoate at seven dosage levels (ranging from 40 mM to 100 mM). An induction of mitotic gene conversions was observed which demonstrated a significant dose-response relationship and a positive mutagenic effect.[7]

Hanna and Dyer (37) tested dimethoate in two bacterial systems by adding 5 to 10 ul of dimethoate to a layer of the bacterial strain. Positive results were observed in two strains of *Escherichia coli* (*E. coli* WP2 uvrA and *E. coli* WP 67). Negative results were seen in several other *E. coli* and *Salmonella typhimurium* strains.[7]

Mohn (38) studied the effect of dimethoate in *E. coli* K-12/galRs18. Dimethoate was shown to have mutagenic activity. A significant does-response relationship was obtained using five does levels (from 1 to 6×10^{-3} M).[7]

American Cyanamid Co. (39) investigated the mutagenic potential of Dimethoate using several strains of *S. typhimurium* and one strain of *E. coli*. Rat liver microsomal enzymes (S-9) were used for metabolic activation. No mutagenic effects were observed. Doses ranged from 20 to 100 ug/plate.

Shirasu et al. (40 studied the mutagenic effect of dimenthoate in the H17 Rec^+ and R45$^-$ strains of *Bacillus subtilis*. No mutagenic activity was observed under the conditions of the study. The dose of dimethoate used was not given.[7]

Agarwal et al. (41) studied the effect of dimethoate on seed setting and germination in the bean (*Phaseolus vulgaris*). Dimethoate in concentrations of 0.1 and 0.5% by volume were used as foliar sprays on bean plants in four observation plots. The spraying was done at the time of bud initiation. Seeds were then collected and soaked for 48 hours at room temperature. Dimethoate reduced germination 23 to 28% below controls. Chromosomal abnormalities including fragments, stickiness, and anaphase bridge formation were seen in 12.8 to 27.5% of the treated series. No abnormalities were seen in the controls.

Amer and Farah (42) studied the cytological effects of dimethoate on cotton (*Gossypium barbadense*) and beans (*Vicia fada*). Bean seeds were treated at concentrations of 0.5, 0.25, 0.125, and 0.0625% using both pure and formulated (solution containing 40% active ingredient) dimethoate. Cotton seeds were treated with the formulated product at concentrations of 0.25, 0.125, and 0.0625% dimethoate. Both pure and formulated dimethoate greatly inhibited cell division in beans. The mitotic index for bean seeds treated with pure dimethoate ranged from 18.4 (0.5% dimethoate) to 62.6 (0.625% dimethoate) compared with a mitotic index of 94.1 for controls. The mitotic index for beans treated with formulated dimethoate ranged from 8.0 (0.25% dimethoate) to 42.0 (0.0625% dimethoate) compared with 56.4 for controls. Chromosomal abnormalities were also observed for all treated seeds. The percentage of abnormal mitoses in beans induced by formulated dimethoate was much higher than that induced by pure dimethoate.

(b) *Studies on Dimethoate-Induced Mutation In Mammalian Test Systems.* Gerstengarbe (43) investigated the ability of dimethoate to induce dominant-lethal mutations in the mouse (*Mus musculus*). Dimethoate was administered intraperitoneally to male mice of an inbred, AB Jena/Halle strain. One set of mice received a one-time dose of 80 mg/kg, while another group received 6.66 mg/kg daily for 30 days. The treated males were then paired with untreated females. The number of implantations, resorptions, and living and dead fetuses on the eighteenth day of gestation was determined. The living fetuses were weighed and separated according to sex. A significant increase in the resorption rate was detected, indicating damage during spermiogenesis. A significant increase was observed in the mutation index indicating that dimethoate, in the case of AB Jena/Halle mice, induces dominant-lethal mutations and is capable of reaching germinal tissue.

[7] The author(s) did not indicate whether a metabolic activation system had been included in the test procedures.

[7] The author(s) did not indicate whether a metabolic activation system had been included in the test procedures.

Bhunya and behera (44) injected adults of both sexes of the mouse (*Mus musculus*) with 1 cc/100 g body weight of dimethoate (0.5 and 1.0% solutions). Control animals were injected with distilled water, and standard cytological slides were prepared from bone marrow cells of animals sacrificed at 24, 48, and 72 hours after treatment. The authors stated that in the treated animals, in addition to other aberrations, centromeric fission and stretching were predominant. The number of chromosomes with breakage at the centromere ranged from 1 to 38 per cell. The frequency of aberrations was highest at 24 hours, moderate at 48 hours, and least after 72 hours for both doses tested. Aberration rates in control animals were not reported.

The Working Group concludes that the the Gerstengarbe (43) study demonstrates that dimethoate can, under certain conditions, reach germinal tissue in mammals. Based on this finding and the other positive mutation results in tests with fungi, bacteria, plants, and mice, the Working Group recommends that a rebuttable presumption be issued against dimethoate pursuant to 40 CFR Section 162.11(a)(3)(ii)(A).

B. *Reproductive and Fetotoxic Effects in Mammalian Species.* 40 CFR 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise if a pesticide "(p)roduces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety." This section reflects concern that chronic exposure to chemicals may result, among other things, in injury to the reproductive system and/or the fetus and provides that a rebuttable presumption shall arise if chronic chemical exposure in test animals produces such results.

Budreau and Singh (45) studied the effect of dimethoate on the reproduction of Charles River CD-1 mice. The insecticide was added to drinking water at the rate of 60 ppm (⅙ the LD_{50}) for five generations. Reproductive performance was evaluated by mating success and reproduction time. Mating success was calculated as the proportion of the females mated that had litters, expressed in percentage. Reproduction time was the number of elapsed days from the first day when the females were presented to the male to the day of delivery. The authors stated that dimethoate treatment significantly reduced mating success and increased reproduction time.

Second litter mating success ranged from 33 to 61% ($p<0.01$) and treated females required significantly longer periods than controls ($p<0.01$) to produce first litters in all generations. Survival rate of total pups and litters was significantly reduced ($p<0.01$) in generations I, III, IV, and V. Histologic examination of the mammary glands of treated females with high newborn mortality showed the glands were well developed and contained milk. The growth rate of dimethoate-treated pups usually fell behind that of controls from day 12 after birth. On day 28, average weight was not always significantly different from controls, mainly because low-weight pups died.

In a dam-transfer experiment (45), a number of control young were transferred from an untreated to a treated, lactating mother. Increased mortality was noted in the young nursed by the treated mothers as compared with controls. This suggested that dimethoate or a toxic metabolite was passed to the young via milk.

Scheufler (46) administered a single 40 mg/kg dose of dimethoate, intraperitoneally, to female AB Jean/Halle mice on the day of conception. On the ninth day of pregnancy the author observed a significant increase in the number of dead embryos ($p<0.01$). When dimethoate was injected daily, at 40 mg/kg, during the first 14 days of pregnancy, four times as many implanted embryos died in comparison to controls. When 40 mg/kg of dimethoate was administered to female C57BL mice, the number of nonpregnant females was increased to 70% as compared to 20 to 30% for controls. When dimethoate was applied to DBA-mice, 50% of the mated females showed no embryos. The author suggested that dimethoate appears to hinder strongly the development of embryos prior to implantation.

The American Cyanamid Co. (47) conducted a three generation feeding study to determine whether dimethoate would interfere with reproduction or lactation. Albino mice of the CF1 strain were fed diets containing 5, 15, 50, and 0 (control) ppm of dimethoate. Animals were approximately one month old at the start of the test. Weaned pups were fed the same diets as their parents.

For mating purposes one male and two females were housed together. Females were housed alone while they cast and weaned their litters, after which parent animals were mated again. There were two mating periods. The report concluded that "reproduction and lactation performance was good for all groups."

An EPA scientist who reviewed this study agreed with the conclusion that no teratogenic effects were observed. The scientist identified the following data from this study relative to the effect of dimethoate on reproduction. This data, however, is not statistically significant.

Diet (parts per million)	Number of mothers died	Number of mothers with tremors or a litter which died
0	1	0
5	[1]2	0
50	2	4

[1] 1 had an abscessed uterus.

Mating record

	F1 generation	F2 generation
1st generation.	All conceived.	1 5 p/m did not conceive.
2d generation..	1 5 p/m did not conceive.	Do. 2 15 p/m did not conceive. 2 50 p/m did not conceive.

In order to determine whether a rebuttable presumption should be issued based on reproductive and fetotoxic effects pursuant to Section 162.11(a)(3)(ii)(B), the Working Group must determine whether an ample margin of safety exists between the levels of dimethoate which produce reproductive and fetotoxic effects and the levels to which humans can reasonably be anticipated to be exposed.

In order to determine whether an ample margin of safety exists, the Working Group must first determine how much dimethoate a woman could be exposed to through: (1) Oral exposure, (2) dermal exposure, or (3) inhalation exposure. For each of these analyses the Working Group assumes a woman to weigh 50 kg. The Working Group is aware that this is a conservative assumption.

(1) *Oral Exposure.* For purposes of this analysis the Working Group assumes dimethoate residues to be present at tolerance level (see Section I.D). The Working Group realizes, however, that residues found in or on raw agricultural commodities are typically lower than tolerance levels. The following calculations are based on the average values for the amount of food eaten per day (1.5 kg) as reported by Lehman (54).

Food	Food factor (percent)	Tolerance (milligrams per kilogram) (40 CFR 180.204)	Contribution to daily intake (milligrams per kilogram)
Alfalfa	[1]		
Apples	1.81	2	0.0362
Beans (dry)	0.50	2	.0100
Beans (snap and lima)	.74	2	.0148
Broccoli	.19	2	.0038
Cabbage	.49	2	.0098
Cauliflower	.43	2	.0086
Celery	.76	2	.0152
Citrus (including grapes, lemons, oranges, tangerines)	3.66	2	.0732
Collards	[2]		
Endive (escarole)	[3]		
Grapefruit	[4]		
Kale	.14	2	.0028
Lemons	[4]		
Lettuce (including mustard greens, endive/escarole)	[5] 1.15	2	.0230
Oranges	[4]		
Pears	.32	2	.0064
Peas (dry)	.12	2	.0024
Peas (fresh)	.49	2	.0098
Peppers	.25	2	.0050
Soybean forage	[1]		
Soybean hay	[1]		
Spinach	.29	2	.0058
Swiss chard (as beets)	.44	2	.0088
Tangerines	[4]		
Tomatoes	3.34	2	.0668
Turnips (roots and tops)	[2]		
Wheat (green fodder and straw)	[1]		
Corn fodder	[1]		
Grapes	.32	1	.0032
Melons	1.98	1	.0198
Potatoes	7.00	0.2	.0140
Cotton/safflower/soybean (as edible oil and margarine)	1.43	.1	.0014
Pecans (as nuts)	.60	.1	.0006
Sorghum grain and forage	[1]		
Corn	1.19	.1	.0012
Corn (as flour/cereal/starch)	.71	.1	.0007
Wheat grain (as flour)	8.05	.04	.0032
Wheat grain (as cereal)	.18	.04	.0001
Eggs	3.0	.02	.0006
Beef	4.60	.02	.0009
Hogs	2.89	.02	.0006
Horses	[6]		
Poultry	2.45	.02	.0005
Sheep	.28	.02	.0001
Milk	19.6	.002	.0004
Total			.35

[1] No food factor available. Exposure is reflected in part by meats and poultry.
[2] See kale.
[3] See lettuce.
[4] See citrus.
[5] See kale/spinach.
[6] Data not available.

The quantity of dimethoate in the average daily diet equals the average daily intake of dimethoate multiplied by the average daily food intake: 0.35 mg×1.5 kg=0.525 mg.

The theoretical exposure of an average woman equals the amount absorbed divided by the weight of the average woman: 0.525 mg/50kg=0.0105 mg/kg of body weight.

(2) *Dermal Exposure.* In order to conduct this analysis the Working Group must make certain assumptions concerning the amount of dimethoate which would come in contact with the skin and how much of this would be absorbed.

Sanderson and Edson (7) studied the dermal absorption characteristics of ^{32}P-labeled dimethoate on the rat. Three to four percent of an applied dose was absorbed after one hour, and 10 to 25% after four hours. On the basis of these results the authors conducted a series of tests involving skin application of a commercial-type ^{32}P-labeled dimethoate formulation using human subjects. The authors found that, after two hours of contact, almost all dimethoate was removed by washing with water. After 5½ hours, 5 to 13% of the dimethoate dose remained after washing with water; however, this was "largely removed" by vigorous washing with soap and water.

For purposes of this analysis, the Working Group will assume that 10% of the dimethoate coming in contact with the skin or clothing of the applicator will be absorbed even after washing.

The Working Group feels that more women of childbearing age would be exposed to dimethoate through application around the home than under any other situation. The Working Group has selected a product representative of a pesticide product containing dimethoate which can be used around the home. This product contains 23.4 percent dimethoate as formulated (equivalent to 2 pounds of dimethoate per gallon). For dermal exposure from spraying, the conservative assumption is made that no applicator would get more than one pint of dilute spray on herself during spraying. This would be enough to thoroughly wet the operator's clothing. The following calculations of exposure assume a dilution for spraying of 16 fluid ounces (or 0.25 pound) of formulated product per 24 pints of water.

Changing pounds to grams gives: 0.25 lb/24 pt×454 gr/lb=4.73 gr/pt. The Working Group has assumed 1 pint exposure and 10 percent absorption by a 50 kg female. To determine the amount absorbed, multiply the amount of dimethoate per pint by the amount absorbed: 4.73 gr×10 percent=0.473 gr=473 mg exposure.

The theoretical exposure of an average woman equals the amount absorbed divided by the weight of the average woman: 473 mg/50 kg=9.46 mg/kg of body weight.

(3) *Inhalation Exposure.* Inhalation exposure from spraying is estimated by assuming that some fraction of the spray enters the breathing zone of the applicator. With

the course spray droplets resulting from a home garden spray nozzle, there is no substantial upward diffusion, and the spray droplets follow a mechanical trajectory to the ground. Since the sprayer is held roughly waist high, normally very little spray would enter the breathing zone. The applicator is thus exposed to substantially less dimethoate by respiration than by dermal contact. This reasoning is in agreement with Wolfe's (55) comment, "over 97 percent of the pesticide to which the body is subjected during most exposure situations, and especially to applicators of liquid sprays, is deposited on the skin." Thus even with the conservative assumption that all inhaled dimethoate would be retained in the lungs of the applicator, it appears that inhalation exposure would not make an important contribution to the total potential exposure.

Total theoretical exposure from dimethoate equals

0.0105 mg/kg (due to oral exposure)
9.4600 mg/kg (due to dermal exposure)
9.4705 mg/kg = total theoretical exposure.

The theoretical margin of safety for dimethoate-induced reproductive and fetotoxic effects equals the effect level divided by the total theoretical exposure level:

$$\frac{20 \text{ mg/kg (Budreau \& Singh (45))}}{9.4705 \text{ mg/kg (total theoretical exposure)}} = 2.11$$

It is generally recognized that humans vary in their susceptibility to a toxicant and that humans may, for a variety of reasons, be far more sensitive than laboratory animals. Therefore, and lacking information to the contrary, the Working Group feels that 2.11 does not constitute an adequate margin of safety and recommends that a rebuttable presumption be issued against dimethoate pursuant to 40 CFR 162(a)(3)(ii)(B).

Registrants and other interested persons can, during the course of the RPAR process, submit data and/or comments regarding the existence of an ample margin of safety for dimethoate-induced reproductive and fetotoxic effects, and any other comments and data concerning dimethoate-induced reproductive and fetotoxic effects.

IV. OTHER RELEVANT ADVERSE EFFECTS

This section addresses certain criteria for determination of unreasonable adverse effects which dimethoate may produce, but for which insufficient evidence exists to initiate a rebuttable presumption.

A. *Delayed Neurotoxicity.* American Cyanamid Co. (48) performed demyelination studies for dimethoate and its oxygen analog, dimethoxon, in white leghorn hens estimated to be 1 to 2 years of age. Although the results appear to show that these chemicals did not cause myelin degeneration, a closer examination of these reports indicates that the tests were inconclusive for the following reasons:

1. An LD_{50} for 24 hours, instead of 7 days, should have been used in the tests;

2. Since hens were given the chemicals in their feed, the dose received by each hen was not accurately known. Administration of the test substance should have been by intubation or gelatin capsule; and

3. Since maximum doses of only one-eighth LD_{50} were administered, delayed neurotoxic effects may not have developed.

The regimen of the study was such that it would not detect delayed neurotoxicity of some compounds that are known to cause this effect. Either much higher doses, i.e., the maximally tolerated dose using atropine, or sub-acute studies for longer periods of time should have been used.

The Agency is not now presuming against dimethoate on the basis of this study but requests any interested party possessing information relevant to this or any other chronic or delayed toxic effect due to dimethoate to submit such data to the Agency.

B. *Synergism.* Uchida et al. (49) have reported on synergism of dimethoate by EPN in mammals and insects. (Synergism is defined as the greater toxicity of two compounds together than would be anticipated from the sum of their individual effects.)

The authors found that one-half the LD_{50} of dimethoate (170 mg/kg) and one-half the LD_{50} of EPN (11 mg/kg) killed an average 90 percent of mice in two trials when given simultaneously. For guinea pigs, the authors found that one-half the LD_{50} of dimethoate (390 mg/kg) and one-half the LD_{50} of EPN (14 mg/kg) killed an average of 24 percent ±5 in five trials when given simultaneously. The authors described this result as "moderate" synergism. The authors noted that EPN blocks liver degradation of dimethoate profoundly in the mouse and less so in the guinea pig and concluded this inhibition in metabolism or detoxification of dimethoate accounted for the synergistic activity in the mouse in the guinea pig.

In a study on the degradation of dimethoate by the human liver, Uchida and O'Brien (16) noted that mammalian amidase is very sensitive to EPN in vivo and that its inhibition should lead to synergistic toxicity in man.

The 1969 Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health (Mrak Report) (50) discussed the synergistic activity of EPN on dimethoate and recommended that "[a]dditional studies should be conducted to evaluate the significance of aliesterase inhibition in man and especially liver aliesterase; and to study the relation between aliesterases and amidases." The report also stated, "In light of present knowledge, studies on the inhibition of plasma and liver aliesterase should be required on all anticholinesterase pesticides."

Although there are no registered products which contain both EPN and dimethoate, these chemicals do have certain use patterns in common. These include use on apples, beans, cotton, grapes, pears, pecans, and tomatoes. The Working Group does not know if it is common practice to mix dimethoate with EPN or to apply them together. The Agency is not now presuming against dimethoate on the basis of these studies but requests registrants and any other interested party possessing information relevant to the use of EPN with dimethoate, or to the synergism of dimethoate by EPN or any other pesticide to submit such data to the Agency.

DIMETHOATE: POSITION DOCUMENT 1

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* References marked with an asterisk are protected from unauthorized duplication by copyright. A copy of the Position Document and all references are available for public inspection in the Office of Special Pesticide Reviews (WH–566), Office of Pesticide Programs, Environmental Protection Agency, East Tower, Room 447, 401 M Street SW., Washington, D.C. 20460.

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**** PRODUCT SEARCH LISTING ****

06/28/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* CC0148	THOMPSON-HAYWARD CHEMICAL COMPANY BOX 2383 KANSAS CITY KS 66110

********** PRODUCT NAME **********

**05207* DE-FEND 8 DLST

**07496* DE-FEND E-267 SYSTEMIC INSECTICIDE

**07497* DE-FEND E-267 SYSTEMIC INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* 000239	CHEVRON CHEMICAL COMPANY ORTHO DIVISION 940 HENSLEY WAY RICHMOND CA 94801

********** PRODUCT NAME **********

**04163* CYGON 267

**04165* ORTHO CYGON 267

REGISTRANT	*NAME AND ADDRESS*
* 000241	AMERICAN CYANAMID COMPANY BOX 400 PRINCETON NJ 08540

********** PRODUCT NAME **********

**03825* CYGON 2E SYSTEMIC INSECTICIDE

**03883* CYGON 267 SYSTEMIC INSECTICIDE

**** PRODUCT SEARCH LISTING ****

06/28/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 000829	SOUTHERN AGRI INSECT INC PO BOX 218 PALMETTO FL 33561

********** PRODUCT NAME **********

**06759* SA-50 BRAND DIMETHOATE INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* 003468	SCHALL CHEMICAL INC BOX 962 MONTEVISTA CO 81144

********** PRODUCT NAME **********

**04561* DIMETHOATE -SULFUR WITH ZINC CARRIER

**04562* DIMETHOATE-SULFUR

**04563* DIMETHOATE-MANEB-SULFUR

REGISTRANT	*NAME AND ADDRESS*
* 005481	AMVAC CHEMICAL CORP 4100 EAST WASHINGTON BLVD LOS ANGELES, CA 90023

********** PRODUCT NAME **********

**02837* DURAGON 8 DLST

**07504* DURHAM DURAGON 2.67 SYSTEMIC INSECTICIDE

**07507* DURHAM DURAGON 25 WP SYSTEMIC INSECTICIDE

**** PRODUCT SEARCH LISTING ****

06/28/77

**CONTINUE REGISTRANT 000481

**007511* DURHAM DURAGON 2.67 SYSTEMIC INSECTICIDE

REGISTRANT *NAME AND ADDRESS*

* CC5905 HELENA CHEMICAL CO
CLARK TOWER, 5100 POPLAR AVE, SUITE 2904
MEMPHIS TN 38137

********** PRODUCT NAME **********

**030086* DIMETHOATE 267 EC

**078663* DIMETHOATE 267 EC

**079947* HOOPER CUST

REGISTRANT *NAME AND ADDRESS*

* CC7478 CHEM PAK COMPANY
10402 S. W. 185TH TERRACE
SOUTH MIAMI FL 33157

********** PRODUCT NAME **********

**080027* CYGON 2E

REGISTRANT *NAME AND ADDRESS*

* CC5219 CLUTCH CHEMICALS, INC
476 HESTER STREET
SAN LEANDRO, CA 94577

********** PRODUCT NAME **********

**** PRODUCT SEARCH LISTING ****

06/28/77

**CONTINUE REGISTRANT 009419

**045834* DIMATE 2E

REGISTRANT *NAME AND ADDRESS*

* 010565 CALIFORNIA DEPT OF AGRICULTURE
WEED & VERTEBRATE PEST CONTROL 1220 N ST
SACRAMENTO CA 95814

********** PRODUCT NAME **********

**100039* ANY APPROPRIATE PRODUCT

**100040* ANY APPROPRIATE PRODUCT

**100041* ANY APPROPRIATE PRODUCT

**100042* ANY APPROPRIATE PRODUCT

**100043* ANY APPROPRIATE PRODUCT

REGISTRANT *NAME AND ADDRESS*

* 011369 BAKERSFIELD AG CHEM INC
PO BOX 5062
OILDALE CA 93308

********** PRODUCT NAME **********

**CE7758* EAC CYMATE 267

**CE7774* EAC CYMATE 25W

**** PRODUCT SEARCH LISTING ****

06/28/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 011656	WESTERN FARM SERVICE INC SHELL CHEM COMPANY 1025 CONNECTICUT AVE-STE 200 WASH DC 20036

********** PRODUCT NAME **********

**059906* DIMETHOATE TOXAPHENE .5-3 EC

REGISTRANT	*NAME AND ADDRESS*
* 021275	SPALDING INC 1921 5TH AVE S ST PETERSBURG FL 33733

********** PRODUCT NAME **********

**05540* X-CEL CYGON 2E

REGISTRANT	*NAME AND ADDRESS*
* 032222	SOUTHERN CHEMICALS, INC. 204 N. ELM AVE, BOX 1480 SANFORD, FL 32771

********** PRODUCT NAME **********

**07121* DIMETHOGON 267 EC

**** PRODUCT SEARCH LISTING ****

06/28/77 APPLICANTS FOR REGISTRATION OF PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 037843	UNIVERSITY OF HAWAII-CC-CP EXTENSION SERV-ENTOMOLOGY BRANCH HONOLULU, HI 96822

********** PRODUCT NAME **********

**08582* DIMETHOATE (L)

REGISTRANT	*NAME AND ADDRESS*
* 028655	N.Y.S. COLLEGE OF AGRICULTURE & LIFE SCIENCES CORNELL UNIV. ITHACA, NY 14853

********** PRODUCT NAME **********

**10423* AYS-DEWEY-DIMETHOATE (CYGON)

**10437* AYS-DEWEY-DIMETHOATE-II

**10465* AYS-DEWEY-DIMETHOATE

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT *NAME AND ADDRESS*

* 000070 RIGO COMPANY, INC.
1200 FORT WAYNE NAT'L BANK BLDG.
FORT WAYNE, IN 46802

********** PRODUCT NAME **********

**00113* KILL-KO CYGON 2-E SYSTEMIC INSECTICIDE

REGISTRANT *NAME AND ADDRESS*

* 000134 HESS AND CLARK DIV OF RHODIA INC
ASHLAND OH 44805
ASHLAND, OH 44805

********** PRODUCT NAME **********

**00057* HESS & CLARK RESIDUAL FLY SPRAY 2 EG

REGISTRANT *NAME AND ADDRESS*

* 000148 THOMPSON-HAYWARD CHEMICAL COMPANY
BOX 2383
KANSAS CITY KS 66110

********** PRODUCT NAME **********

**00865* DE-FEND E-267 DIMETHOATE SYSTEMIC INSECTICIDE

**00870* DIMETHOATE TECHNICAL

**00877* DE FEND E-200 DIMETHOATE SYSTEMIC INSECTICIDE

**00883* DE-FEND W-25 INSECTICIDE

**01131* DE-FEND-70X

**** PRODUCT SEARCH LISTING ****

06/28/77

**CONTINUE REGISTRANT 000148

**01222* DE-FEND TECHNICAL

REGISTRANT *NAME AND ADDRESS*

* 000239 CHEVRON CHEMICAL COMPANY
ORTHO DIVISION 940 HENSLEY WAY
RICHMOND CA 94801

********** PRODUCT NAME **********

**02225* ORTHO CYGON 267 SYSTEMIC INSECTICIDE,

REGISTRANT *NAME AND ADDRESS*

* 000241 AMERICAN CYANAMID COMPANY
BOX 400
PRINCETON NJ 08540

********** PRODUCT NAME **********

**00075* CYGON* TECHNICAL INSECTICIDE (FOR MANUFACTURING PURPOSE ONLY)

**00082* CYGON 2-E INSECTICIDE

**00094* CYGON 267 SYSTEMIC INSECTICIDE

**00175* CYGON SYSTEMIC 25 INSECTICIDE

**00210* CYGON V FLY SPRAY

**00218* CYGON SC-9 SYSTEMIC INSECTICIDE

**00231* CYGON CONCENTRATE SYSTEMIC INSECTICIDE FOR FORMULATION OF CYGON

**00233* CYGON 400 SYSTEMIC INSECTICIDE

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 000279	FMC CORP. AGRICULTURAL CHEM DIV. 100 NIAGARA ST. MIDDLE PORT NY 14105

**** PRODUCT NAME ****

**02821* NIAGARA DIMETHOATE 267 SYSTEMIC INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* 000523	ROBERTS LAB DIV HOPKINS AGR CHEM 4995 N MAIN ST ROCKFORD IL 61101

**** PRODUCT NAME ****

**00054* CYGON 2-E SYSTEMIC INSECTICIDE

**00079* FLYGON 2-E SYSTEMIC INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* 000538	SCOTT O M & SONS COMPANY MARYSVILLE OH 43040

**** PRODUCT NAME ****

**00135* STOP INSECTS BEFORE THEY START

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 000572	ROCKLAND CHEMICAL CO. INC. P.O. BOX 909 CALDWELL, NJ 07006

**** PRODUCT NAME ****

**00224* I.B.A. RESIDUAL FLY SPRAY 8

REGISTRANT	*NAME AND ADDRESS*
* 000602	RALSTON PURINA COMPANY CHECKERBOARD SQUARE ST LOUIS MO 63188

**** PRODUCT NAME ****

**00107* CYGON PURINA 2-E SYSTEMIC INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* 000635	E-Z FLO CHEMICAL CO. DIV. OF GROWER SERVICE CORP. P.O. BOX 808 LANSING, MI 48901

**** PRODUCT NAME ****

**00666* E-Z FLO DIMETHOATE EC

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT *NAME AND ADDRESS*

* 000655 PRENTISS DRUG & CHEMICAL COMPANY INC
363 7TH AVE
NEW YORK NY 10001

********** PRODUCT NAME **********

**00445* PRENTOX DIMETHOATE TECHNICAL

REGISTRANT *NAME AND ADDRESS*

* 000904 PRATT B G
DIV GABRIEL CHEM LTD 204 21ST AVE
PATERSON NJ 07505

********** PRODUCT NAME **********

**00179* PRATT CYGON 2-E SYSTEMIC INSECTICIDE

REGISTRANT *NAME AND ADDRESS*

* 001029 AIDEX CORPORATION
P.O. BOX 7349
OMAHA, NB 68107

********** PRODUCT NAME **********

**00004* VAP-O-ATE

**00108* DIMEX 267 SYSTEMIC INSECTICIDE

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT *NAME AND ADDRESS*

* 001386 UNIVERSAL COOPERATIVES INC
PO BOX 836
ALLIANCE OH 44601

********** PRODUCT NAME **********

**00445* CYGON 2-E

**00585* UNICO CYGONA FLY SPRAY

REGISTRANT *NAME AND ADDRESS*

* 002217 PBI-GORDON CORPORATION
300 SO 3RD ST
KANSAS CITY KS 66118

********** PRODUCT NAME **********

**00495* CYGON 2-E FLY SPRAY SYSTEMIC INSECTICIDE

REGISTRANT *NAME AND ADDRESS*

* 002342 KERR-MCGEE CHEMICAL CORP
MGR PKG & LABELING
KERR-MCGEE CENTER
OKLAHOMA CITY OK 73102

********** PRODUCT NAME **********

**00758* GRO-TONE CYGON

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 002724	ZOECON INDUSTRIES, INC. 12206 DENTON DRIVE DALLAS, TX 75234

********** PRODUCT NAME **********

**00138* STARBAR DIMOX EMULSIFIABLE CONCENTRATE

**00140* STARBAR GOLDEN MALRIN LIQUID EMULSIFIABLE CONC.

REGISTRANT	*NAME AND ADDRESS*
* CC2749	ACETO CHEMICAL COMPANY INC 126-02 NORTHERN BLVD FLUSHING NY 11368

********** PRODUCT NAME **********

**00041* DIMETHOGON 267 EC

**CC042* DIMETHOGON 2E

**00046* DIMETHOATE TECHNICAL

**00134* DIMETHOGON 25% WETTABLE POWDER SYSTEMIC INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* 002935	WILBUR ELLIS CO. P. O. BOX 1286 FRESNO, CA 93715

********** PRODUCT NAME **********

**CC390* RED-TOP DIMETHOATE 2.67 SPRAY

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 004691	PHILLIPS ROXANE INC 2621 N BELT HIGHWAY ST JOSEPH MO 64502

********** PRODUCT NAME **********

**CCC90* DIMETHOATE BARN & PREMISE SPRAY

REGISTRANT	*NAME AND ADDRESS*
* 005481	AMVAC CHEMICAL CORP 4100 EAST WASHINGTON BLVD LOS ANGELES, CA 90023

********** PRODUCT NAME **********

**CCC54* ALCO CYGON 2 E

**00102* DURHAM DURAGON 2.67 SYSTEMIC INSECTICIDE

**00133* DURHAM DURAGON 25 WP SYSTEMIC INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* 005602	HUB STATES CORPORATION 2002 NORTH ILLINOIS STREET INDIANAPOLIS IN 46202

********** PRODUCT NAME **********

**CCC61* HUB STATES CYGON 2E

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* 003905	HELENA CHEMICAL CO CLARK TOWER, 5100 POPLAR AVE, SUITE 2904 MEMPHIS TN 38137

********** PRODUCT NAME **********

**002C7* CYBROM - E.C.

**00212* HELENA ANIMAL HEALTH CYGON 2-E SYSTEMIC INSECTICIDE

REGISTRANT	*NAME AND ADDRESS*
* CC7C01	OCCIDENTAL CHEMICAL CC P O BOX 198 LATHROP, CA 95330

********** PRODUCT NAME **********

**00187* DIMETHOATE 2.67 EC

REGISTRANT	*NAME AND ADDRESS*
* CC7173	CHEMPAR CHEMICAL COMPANY INC 250 MADISON AVE NEW YORK NY 10016

********** PRODUCT NAME **********

**00087* CHEMPAR DIMETHOATE TECHNICAL (FORM MANUFACTURING PURPOSES ONLY)

**00115* CHEMPAR DIMETHOATE 2.67 EC

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

REGISTRANT	*NAME AND ADDRESS*
* CC7273	CROWN CHEMICAL INCORPORATED 4995 NORTH MAIN STREET ROCKFORD IL 61101

********** PRODUCT NAME **********

**C0055* CROWN CYGON 2-E SYSTEMIC INSECTICIDE

**C0140* FLYBAN 2-E

REGISTRANT	*NAME AND ADDRESS*
* CC7401	VOLUNTARY PURCHASING GROUP INC PO BOX 450 BONHAM TX 75418

********** PRODUCT NAME **********

**00097* FERTI-LOME SYSTEMIC EVERGREEN SPRAY

**CC1C6* FERTI-LOME SPIDER MITE SPRAY

REGISTRANT	*NAME AND ADDRESS*
* 007569	BASF WYANDOTTE CORPORATION PO BOX 181 100 CHERRY HILL RD PARSIPPANY NJ 07054

********** PRODUCT NAME **********

**C0030* REBELATE SYSTEMIC INSECTICIDE

**00032* PERFEKTHION MANUFACTURERS' CONCENTRATE

**0CC38* REBELATE 2E DIMETHOATE SYSTEMIC INSECTICIDE

REGISTRANT *NAME AND ADDRESS*

* 008590 AGWAY INC
CHEMICAL DIV BOX 1333
SYRACUSE NY 13201

********** PRODUCT NAME **********

**CC200* CYGON 2-E SYSTEMIC INSECTICIDE

REGISTRANT *NAME AND ADDRESS*

* 009319 CUSTOM CHEMICALS, INC
476 HESTER STREET
SAN LEANDRO, CA 94577

********** PRODUCT NAME **********

**00010* DIMATE 267 DIMETHOATE SYSTEMIC INSECTICIDE

REGISTRANT *NAME AND ADDRESS*

* 009779 RIVERSIDE CHEM COMPANY
P.O. BOX 171199 855 RIDGE LAKE BLVD
MEMPHIS TN 38117

********** PRODUCT NAME **********

**0C206* RIVERSIDE DIMATE 2.67

REGISTRANT *NAME AND ADDRESS*

* 010162 GOWAN COMPANY
P.O. BOX 5696
YUMA, AZ 85364

********** PRODUCT NAME **********

**00055* PROKIL METHOATE W-25 INSECTICIDE

**0C056* PROKIL DIMETHOATE E-267

REGISTRANT *NAME AND ADDRESS*

* 011885 CENTRAL SOYA COMPANY INC
1300 FORT WAYNE BANK BLDG
FT WAYNE IN 46802

********** PRODUCT NAME **********

**0CC02* MASTER MIX CYGON 2-E

REGISTRANT *NAME AND ADDRESS*

* 013801 REGISTRATION CONSULTING ASSOC.
C/O CHARLES C. YEAGER
9 WEST KNOLL ROAD
ANDOVER, MA 01810

********** PRODUCT NAME **********

**0CC01* DIMETHOATE TECHNICAL

**** PRODUCT SEARCH LISTING ****

06/28/77 FEDERALLY REGISTERED PRODUCTS CONTAINING DIMETHOATE

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REGISTRANT *NAME AND ADDRESS*

* 012660 I PI CI S P A
VIA FRATTELLI BELTRAMI 11
NOVATE MILANESE, ITALY 00000

********** PRODUCT NAME **********

**000012* DIMETHOATE TECHNICAL

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REGISTRANT *NAME AND ADDRESS*

* 026780 UNITED FARMERS BUYING SERVICE, INC.
ROUTE 1
DEFOREST, WI 53532

********** PRODUCT NAME **********

**000004* DIMETHOATE 267 E.C. SYSTEMIC INSECTICIDE

[FR Doc.77-26195 Filed 9-9-77;8:45 am]

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